JAPANESE [JP,06-087750,A]

CLAIMS DETAILED DESCRIPTION TECHNICAL FIELD EFFECT OF THE INVENTION TECHNICAL PROBLEM MEANS EXAMPLE

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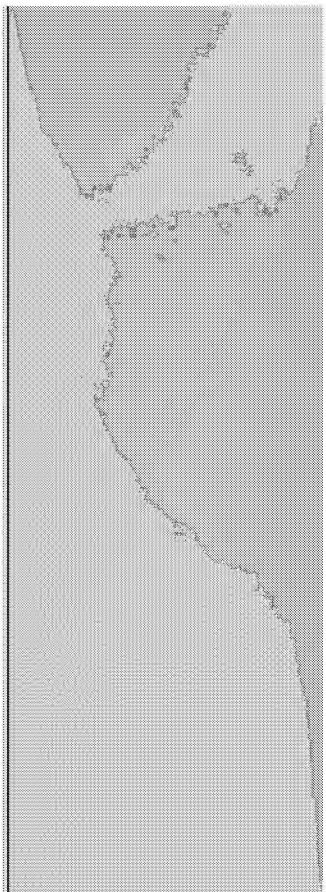
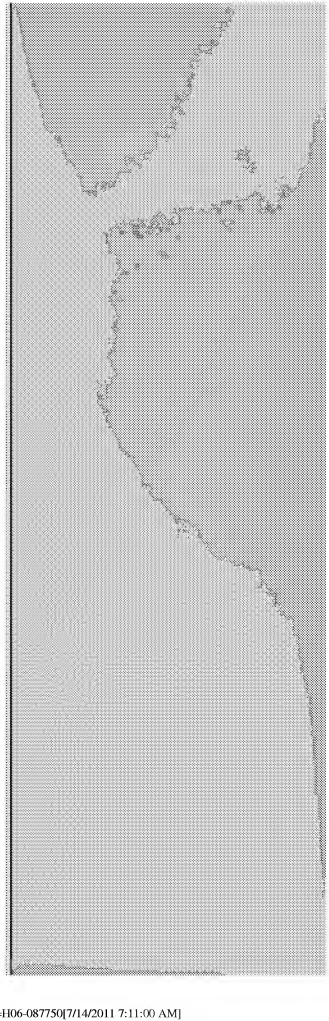


* NOTICES *

DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Industrial Application]This invention relates to the medicinal composition which contains stable 1 alpha and 25-dihydroxycholecalciferol to heat etc.
[0002]
[Description of the Prior Art]Vitamin D_3 receives a metabolic turnover in the living body, and 1 alpha and carbon of the 25th place in the structure are hydrogenated, it becomes 1 alpha and 25-dihydroxycholecalciferol, and it is said that this demonstrates physiology activity. In the present, this 1 alpha and 25-dihydroxycholecalciferol have obtained high evaluation on Medical Science Division to the vitamin D metabolic error patient as a living body's original active-vitamin-D_3.
[0003]However, since activity would fall if the pharmaceutical preparation in which 1 alpha and 25-dihydroxycholecalciferol are unstable to heat, air, humidity, and light, oxidize easily, and are generally used is saved as it is, methods, such as using an aluminum bag package in order to intercept humidity and light conventionally, were taken.
[0004]However, heat and stability to air could not be secured but such a method of stability was insufficient.
[0005]
[Problem to be solved by the invention]Therefore, it does not have the fault which was described above but development of the pharmaceutical preparation which can secure sufficient stability whose prolonged preservation is attained was demanded.
[0006]
[Means for solving problem]In this actual condition, as a result of inquiring wholeheartedly, by blending with 1 alpha and 25-dihydroxycholecalciferol pharmaceutical preparation by making tocopherol into stabilizer, this invention persons found out that the pharmaceutical preparation with which it is satisfied of said demand was obtained, and completed this invention.
[0007]That is, this invention provides the medicinal composition containing 1 alpha, 25-dihydroxycholecalciferol, and tocopherol.
[0008] The tocopherol blended with the medicinal composition of this invention as stabilizer may be isolation tocopherol or a tocopherol derivative, and they may be which homologs, such as alpha, beta, gamma, and sigma. As these tocopherol, DL-alpha-



tocopherol, acetic acid DL-alpha-tocopherol, etc. are mentioned, for example.

[0009]What is necessary is to blend the above-mentioned tocopherol with 1 alpha and 25-dihydroxycholecalciferol which are active principles, and just to pharmaceutical-preparation-ize in accordance with a conventional method, in order to prepare the medicinal composition of this invention.

[0010]1 alpha in this invention medicinal composition, and the loadings of 25-dihydroxycholecalciferol, It is desirable to consider it as the 0.00001 to 0.001 weight % ("%" only shows hereafter) grade, and, as for especially tocopherol, it is preferred to blend 0.05% - about 1% about 0.01 to 5%. Since the effect as stabilizer becomes low when there are few loadings of tocopherol than the above, and a tinctorial change occurs easily when too large, and the commodity value of pharmaceutical preparation may be reduced, neither is preferred.

[0011]Pharmaceutical preparation are prepared by carrying out can be used as various kinds of pharmaceutical forms, for example, a tablet, a granule, subtle granules, hard capsules, an elastic capsule, etc. like the above.

[0012]In these pharmaceutical-preparation-izing, various additive agents usually used for medicinal pharmaceutical preparation-ization can be blended within limits which do not spoil the effect of this invention. For example, crystalline cellulose, milk sugar, starch, mannite, a silicic acid anhydride, Hydroxypropylcellulose, hydroxypropylmethylcellulose, Carboxymethyl-cellulose calcium, magnesium stearate, dehydrated ethanol, medium-chain-fatty-acid triglyceride, corn oil, soybean oil, sesame oil, gelatin, glycerin, D-sorbitol, etc. can be blended and pharmaceutical-preparation-ized.

[0013]

[Working example]Next, although an working example is given and this invention is explained in more detail, this invention is not restrained at all by these working examples.

[0014]Fruit By the example of ** 1 following formula, 1 alpha and 25-dihydroxycholecalciferol pharmaceutical preparation were prepared. 1 alpha and 25-dihydroxycholecalciferol pharmaceutical preparation which were obtained were put into the vial, it kept at 60 **, and the ullage of 1 alpha and 25-dihydroxycholecalciferol was measured temporally. This result is shown in Table 1.

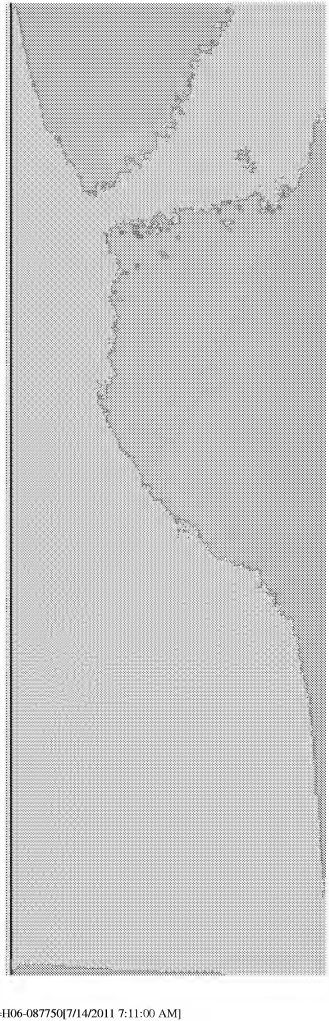
[0015]

(Method of place)

Formula I formula II formula III formula IV. 1 alpha, 25-dihydroKISHIKORE Calciferol (mug). 0.25 0.25 0.25 0.25. Dehydrated ethanol (mg) 0.1 0.1. 0.1 0.1 Acetic acid-DL-alpha-tocopherol (mg) - 0.05 0.1 1.0 medium-chain-fatty-acid TORIGU resaler Ide (mg) 99.9 99.85 99.8 98.9 ** Total (mg) 100 100 100 100

[0016] (Process) 1 alpha and 25-dihydroxycholecalciferol were dissolved in dehydrated ethanol, and the vial was filled up with what was melted in medium-chain-fatty-acid triglyceride with the acetic acid-DL-alpha-tocopherol.

[0017](Join **)



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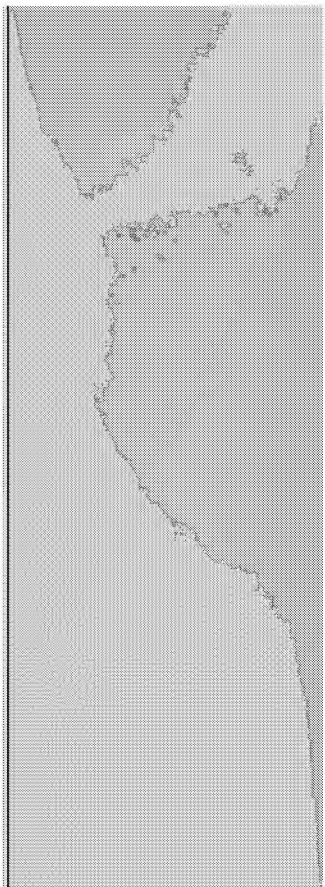

In the pharmaceutical preparation which does not contain the acetic acid-DL-alpha-tocopherol, 1 alpha and 25-dihydroxycholecalciferol will almost decompose by preservation for two weeks so that clearly from this result, but in what blended the acetic acid-DL-alpha-tocopherol, it was hardly decomposed.

[0018]Fruit The elastic capsule was manufactured according to the example of ** 2 following formula.

(Method of place)

1 alpha, 25-dihydroKISHIKORE Calciferol 0.25 mug dehydrated ethanol 0.1 mg DL-alpha-tocopherol 0.1 mg medium-chain-fatty-acid triglyceride 99.8 mg smallness Total 100 mg [0019] Gelatin 62.5 mg concentrated glycerin 12.5 mg D-sorbitol syrup (70%) 9.37 mg titanium oxide 0.63 mg smallness Total 85 mg ** Total 185 mg [0020] (Process) 1 alpha and 25-dihydroxycholecalciferol were dissolved in dehydrated ethanol, and the soft capsule produced with gelatin, concentrated glycerin, D-sorbitol syrup, and titanium oxide was filled up with what was melted in medium-chain-fatty-acid triglyceride with DL-alpha-tocopherol. Even if it saved the obtained elastic capsule six months or more at the room temperature, it was stable.

[0021]

[Effect of the Invention] Since the medicinal composition prepared by this invention can prevent disassembly of 1 alpha and 25-dihydroxycholecalciferol which is an active principle by operation of tocopherol and this can be kept stable, Prolonged preservation is attained and it is very advantageous as medicines for a therapy, such as osteoporosis, a vitamin D metabolic error, chronic renal failure, hypoparathyroidism, rickets, and osteomalacia.

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